

WHAT IS CLAIMED IS:

Sub 1
1. A molecule comprising SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (a) immunospecifically binds CD40, and (b) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.

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2. The molecule of claim 1 comprising the amino acid sequence of SEQ ID NO:2 or the amino acid sequence of SEQ ID NO:7 or the amino acid sequences of both SEQ ID NO:2 and NO:7.

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3. The molecule of claim 1 which is an antibody.

Sub B2
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4. The molecule of claim 1 which is a fusion protein comprising the amino acid sequence of a second molecule that is not an antibody.

5. The molecule of claim 4 that comprises an amino acid sequence of bryodin (BD1) fused to SEQ ID NO:7 fused to SEQ ID NO:2.

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6. The molecule of claim 1 which is an antibody comprising a variable domain of monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, and a human constant region.

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7. The molecule of any one of claims 1-3 which is purified.

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8. A purified protein comprising an amino acid sequence that has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7, which protein (a) immunospecifically binds CD40;

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and (b) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.

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9. A purified protein, which protein (a) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (b) increases the binding of CD40 ligand to CD40 by at least 45%, and (c) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110.

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10. An isolated nucleic acid comprising SEQ ID NO:1, SEQ ID NO:6, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID NO:15.

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11. An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10.

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12. The isolated nucleic acid of claim 11 comprising a nucleotide sequence encoding a protein comprising (a) a heavy chain variable domain of monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, and (b) a human constant region.

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13. An isolated nucleic acid comprising a nucleotide sequence encoding a protein comprising an amino acid sequence that has at least 95% identity to SEQ ID NO:2 or SEQ ID NO:7.

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14. An isolated nucleic acid comprising a nucleotide sequence encoding a protein, which protein competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession

number PTA-110, and which protein increases the binding of CD40 ligand to CD40 by at least 45%.

15. An isolated nucleic acid comprising a nucleotide
5 sequence encoding a fusion protein, said fusion protein
comprising an amino acid sequence of bryodin 1 (BD1) fused to
SEQ ID NO:7 fused to SEQ ID NO:2.

16. An isolated nucleic acid which hybridizes to the
10 reverse complement of a DNA consisting of a coding DNA
sequence encoding a protein consisting of an amino acid
sequence selected from the group consisting of SEQ ID NO:2
and SEQ ID NO:7, under highly stringent conditions, which
isolated nucleic acid encodes a protein that
15 immunospecifically binds CD40.

17. A recombinant cell containing a recombinant nucleic
acid vector comprising a nucleotide sequence encoding a
protein, which protein competes for binding to CD40 with
20 monoclonal antibody S2C5 as secreted by the hybridoma
deposited with the ATCC and assigned accession number PTA-
110, and which protein increases the binding of CD40 ligand
to CD40 by at least 45%.

18. A recombinant cell containing a recombinant nucleic
25 acid vector comprising SEQ ID NO:1, SEQ ID NO:6, SEQ ID
NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, or SEQ ID
NO:15.

19. A method of producing a protein comprising:
30 (a) growing a cell containing a recombinant
nucleotide sequence encoding a protein, which
protein competes for binding to CD40 with
monoclonal antibody S2C6 as deposited with the
ATCC and assigned accession number PTA-110,
35 and which protein increases the binding of

- CD40 ligand to CD40 by at least 45%, such that the protein is expressed by the cell; and
- (b) recovering the expressed protein.

- 5 20. A method of producing a protein comprising:
- (a) growing a cell containing a recombinant nucleotide sequence encoding a protein comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, such that a protein encoded by said nucleotide sequence is expressed by the cell; and
- 10 (b) recovering the expressed protein.

- 15 *put a 4* 21. A pharmaceutical composition comprising:
- (a) a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned
- 20 accession number PTA-110, in an amount effective for the treatment or prevention of cancer; and
- 25 (b) a pharmaceutically acceptable carrier.

- 30 22. A pharmaceutical composition comprising:
- (a) a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number
- 35 PTA-110, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii)

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- 5 comprises one or more substitutions or
insertions in primary amino acid sequence
relative to native monoclonal antibody S2C6 as
secreted by the hybridoma deposited with the
ATCC and assigned accession number PTA-110,
in an amount effective for the treatment or
prevention of cancer; and
- (b) a pharmaceutically acceptable carrier.
- 10 23. A pharmaceutical composition comprising:
- (a) a molecule comprising SEQ ID NO:2, SEQ ID
NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8,
SEQ ID NO:9, or SEQ ID NO:10, which molecule
(i) immunospecifically binds CD40, (ii)
15 increases the binding of CD40 ligand to CD40
by at least 45%, and (iii) comprises one or
more substitutions or insertions in primary
amino acid sequence relative to native
monoclonal antibody S2C6 as secreted by the
hybridoma deposited with the ATCC and assigned
20 accession number PTA-110, in an amount
effective for activating or augmenting an
immune response; and
- (b) a pharmaceutically acceptable carrier.
- 25 24. A pharmaceutical composition comprising:
- (a) a purified protein, which protein (i) competes
for binding to CD40 with monoclonal antibody
S2C6 as secreted by the hybridoma deposited
with the ATCC and assigned accession number
30 PTA-110, (ii) increases the binding of CD40
ligand to CD40 by at least 45%, and (iii)
comprises one or more substitutions or
insertions in primary amino acid sequence
relative to native monoclonal antibody S2C6 as
secreted by the hybridoma deposited with the
35 ATCC and assigned accession number PTA-110,

in an amount effective for activating or
augmenting an immune response; and
(b) a pharmaceutically acceptable carrier.

5 25. The pharmaceutical composition of any one of claims
21-24 further comprising CD40 ligand.

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10 26. A method for the treatment or prevention of cancer
in a subject comprising:
administering to the subject an amount of a
molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ
ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or
SEQ ID NO:10, which molecule (i) immunospecifically
binds CD40, (ii) increases the binding of CD40
ligand to CD40 by at least 45%, and (iii) comprises
15 one or more substitutions or insertions in primary
amino acid sequence relative to native monoclonal
antibody S2C6 as secreted by the hybridoma
deposited with the ATCC and assigned accession
number PTA-110, which amount is effective for the
20 treatment or prevention of cancer.

25 27. A method for the treatment or prevention of cancer
in a subject comprising:
administering to the subject an amount of a
purified protein, which protein (i) competes for
binding to CD40 with monoclonal antibody S2C6 as
secreted by the hybridoma deposited with the ATCC
and assigned accession number PTA-110, (ii)
increases the binding of CD40 ligand to CD40 by at
30 least 45%, and (iii) comprises one or more
substitutions or insertions in primary amino acid
sequence relative to native monoclonal antibody
S2C6 as secreted by the hybridoma deposited with
the ATCC and assigned accession number PTA-110,
35 which amount is effective for the treatment or
prevention of cancer.

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28. A method for activating or augmenting the immune response of a subject comprising:

5 administering to the subject an amount of a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, which molecule (i) immunospecifically binds CD40, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, which amount is such that the immune response of the subject is activated or augmented.

29. A method for activating or augmenting the immune response of a subject comprising:

20 administering to the subject an amount of a purified protein, which protein (i) competes for binding to CD40 with monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, (ii) increases the binding of CD40 ligand to CD40 by at least 45%, and (iii) comprises one or more substitutions or insertions in primary amino acid sequence relative to native monoclonal antibody S2C6 as secreted by the hybridoma deposited with the ATCC and assigned accession number PTA-110, which amount is such that the immune response of the subject is activated or augmented.

30. A method for the treatment or prevention of an immune disorder in a subject comprising:

35 administering to the subject an amount of a molecule comprising SEQ ID NO:2, SEQ ID NO:3, SEQ

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5 ID NO:4, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or
SEQ ID NO:10, which molecule (i) immunospecifically
binds CD40, (ii) increases the binding of CD40
ligand to CD40 by at least 45%, and (iii) comprises
one or more substitutions or insertions in primary
amino acid sequence relative to native monoclonal
antibody S2C6 as secreted by the hybridoma
deposited with the ATCC and assigned accession
number PTA-110, which amount is effective for the
10 treatment or prevention of an immune disorder.

31. A method for the treatment or prevention of an
immune disorder in a subject comprising:
15 administering to the subject an amount of a
purified protein, which protein (i) competes for
binding to CD40 with monoclonal antibody S2C6 as
secreted by the hybridoma deposited with the ATCC
and assigned accession number PTA-110, (ii)
increases the binding of CD40 ligand to CD40 by at
least 45%, and (iii) comprises one or more
20 substitutions or insertions in primary amino acid
sequence relative to native monoclonal antibody
S2C6 as secreted by the hybridoma deposited with
the ATCC and assigned accession number PTA-110,
which amount is effective for the treatment or
25 prevention of an immune disorder.

32. The method of any one of claims 26-31 further
comprising administering CD40 ligand to the subject.

30 33. The method of any one of claims 26-31 in which the
subject is a human.

34. The antibody of claim 3 which is not isotype IgG1.

35 35. A transgenic non-human animal, plant, or an
isolated cell containing one or more transgenes encoding a

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5 protein, which protein competes for binding to CD40 with
monoclonal antibody S2C6 as secreted by the hybridoma
deposited with the ATCC and assigned accession number PTA-
110, and which protein increases the binding of CD40 ligand
to CD40 by at least 45%.

10 36. A pharmaceutical composition comprising in an
amount effective for the treatment or prevention of cancer or
an immune disorder, or for activating or augmenting an immune
response: (a) a molecule that immunospecifically binds CD40,
which molecule increases the binding of CD40 ligand to CD40;
(b) CD40 ligand; and (c) a pharmaceutically acceptable
carrier.

15 37. A method for the treatment or prevention of cancer
or an immune disorder in a subject comprising administering
to the subject, in an amount effective for said treatment or
prevention: (a) a molecule that immunospecifically binds
CD40, which molecule increases the binding of CD40 ligand to
CD40; and (b) CD40 ligand.

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Ab*

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